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Presentation and Attrition in Complex Pulmonary Atresia

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Objectives. **This study summarized patterns of presentation and attrition in complex pulmonary atresia.**

Background. **Assessment of the potential impact of surgical strategies for managing complex pulmonary atresia requires information about variability in age and physiology at presentation of the condition.**

Methods. **We performed a retrospective review of age at presentation, referral source, pulmonary artery and collateral anatomy and surgical history of 218 patients from two institutions dealing with congenital heart disease throughout life.**

Results. **Approximately 65% of pulmonary atresia appears in infancy, with 50% of patients severely symptomatic from cyanosis and 25% from heart failure. Compared with those presenting undiagnosed, patients referred secondarily for specialist management tend to be older when first seen, and care must be taken when generalizing about the natural history of the condition from their survival experience. Overall actuarial survival, including the effects of operation, suggests that 60% (95% confidence limits [CL] 43 to 73) of patients presenting in infancy survive to their first birthday, 65% (95% CL 51 to 74) of those alive at 1 year old survive to the age of 10, and 16% (95% CL 5 to 31) of those alive at 10 years old survive to age 35.**

Conclusions. **Novel surgical approaches have generally been applied beyond infancy in patients selected by their survival through the period of greatest attrition for this disease. Unless successful application in symptomatic infants is demonstrated, we cannot assume that these serial and complicated operations will have a major impact on the outlook of most patients with complex pulmonary atresia.**

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Preoccupation with the "correctability" of complex pulmonary atresia dates from the first conduit repair in 1966 by Ross (1), achieved in a patient with pulmonary atresia and three congenital systemic-pulmonary collateral arteries; the patient still survives but has pulmonary hypertension. This pioneering effort started a trend for surgeons to perform preliminary operations aimed at modifying the intrapericardial and intrapulmonary artery anatomy with a view to ultimate definitive repair—an aspiration constrained over the years by our understanding both of the anatomy and the limitations of surgical intervention in changing it. However, recent optimism has stemmed from some surgical series (2–4), impressive in their dexterity, ingenuity and number of procedures required, in which patients with extremely unpromising pulmonary artery anatomy were brought by a series of operations to successful definitive repair. This has led us to reexamine the patients whom we follow up to establish some impression of the natural history and pattern of presentation of the condition and to assess the implications of these new surgical strategies for our practice.

Methods

We undertook a retrospective review of the records of all patients with pulmonary atresia, ventricular septal defect and a pulmonary blood supply derived exclusively from congenital aortopulmonary collateral arteries. Patients with a duct-dependent pulmonary blood supply were excluded. Two hundred eighteen such patients were seen at the Hospital for Sick Children, Great Ormond Street or the National Heart Hospital, London, or both, in the period from 1965 to 1991. Between them, the two hospitals see patients with congenital heart disease from the neonatal period to late adult life, some transferring from one hospital to the other during adolescence. Over the long time frame of the study, the strategies for investigation and treatment have varied. In particular, there has been an institutional bias since ~1986 at the National Heart Hospital to avoid operation in adolescents and adults in stable condition. Nearly all patients have undergone selective injections into their collateral vessels at some stage, and of the early patients in whom no intrapericardial pulmonary artery was demonstrated at catheterization, many have had an exploratory operation. When first documented, the intrapericardial pulmonary arteries of all patients were classified as absent, hypoplastic or "reasonable," and the number of collateral vessels delineated was counted.

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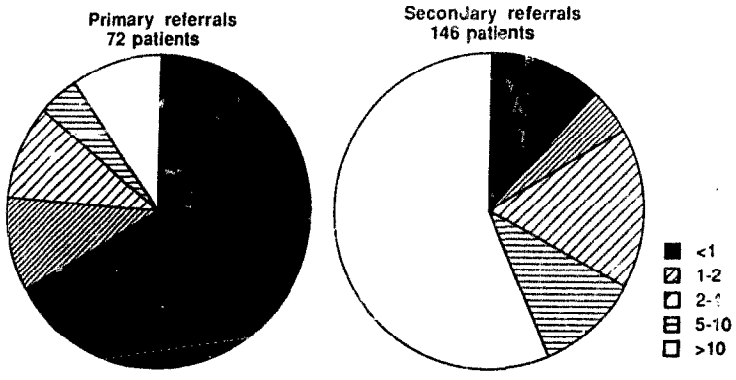

Figure 1. Age at referral (years).

Seventy-two patients who arrived undiagnosed had been referred because of cyanosis or failure to thrive. A further 106 patients with an established diagnosis were referred for specialist management or surgical repair from other cardiologists within the United Kingdom and 40 from cardiologists abroad. The year, age and reason for presentation and the nature and indication for each operation was noted. Indications for a first operation were classified as 1) critical cyanosis; 2) heart failure; 3) elective staging operation toward definitive repair (e.g., elective unifocalization [5]); or 4) definitive repair.

To generate actuarial data, dates of birth, presentation to our practice, surgery and death were obtained. Survival beyond the last contact with our hospitals was not assumed. Endocarditis, cerebral events, aortic regurgitation and late right heart failure were presumed present from the date of first recognition of the complication. Ability index (6) at last contact was recorded.

Statistical methods. Categoric differences were examined using contingency tables, group differences using *t* tests. Survival information was summarized using Kaplan-Meier methodology (7). Generation of summary survival information in a condition where an important proportion of patients present late requires some assumptions. By only allowing patients to contribute to the survival analysis from the date first seen by us (i.e., a patient first seen at age 10 years does not feature in the curve during infancy), we assumed that attrition in early childhood in the units referring patients to us was no better or worse than what we have documented in our own practice. To be clinically useful, survival across infancy, from 1 to 10 years, >10 years and >20 years was examined separately. Possible anatomic features influencing survival through each of these epochs were explored univariately and multivariately using the Cox proportional hazards model (8).

In contrast to variables pertaining at presentation, surgical intervention can influence survival patterns only from the time of operation. Many first operations are undertaken in patients who are severely symptomatic from cyanosis or heart failure. It can well be argued that without operation such patients would die. However, other first operations are undertaken in less symptomatic patients, where the aim is to prepare them for later definitive repair. An attempt was made to assess the impact on long-term survival of such elective surgical strategies initiated in "well balanced" patients. For this exercise, patients undergoing nonelective surgical treatment for severe cyanosis or heart failure were censored at the time of their first operation. The remaining patients were transferred from a "preoperative" to a "postoperative" risk set at the time of the first "staging" operation. Comparison of the preoperative and postoperative hazard estimates generated then allowed comparison of the survival experience of patients of the same age with and without such elective operation. Standard errors for the annual hazard estimates were obtained. This analysis makes the assumption that patients with and without operation are fundamentally similar—that the timing of the first staging operation is "uninformative" from the point of view of survival probability. For the age range beyond infancy, entry to such a staging protocol was then considered a time-dependent covariate in a full Cox proportional hazards model that also included information on referral source, era of presentation (<1980, 1980 to 1985 and >1985), pulmonary artery anatomy and hospital. This analysis provokes conclusions about the hazard early and late after elective operation for patients of the same age, allowing for the other variables in the model.

Similarly, to examine the decision to attempt definitive repair in patients surviving >5 years old, this operation was entered as a time-dependent covariate in a proportional hazards model that also included the previously considered variables and information on age at presentation (infancy, age 1 to 5 years and >5 years). Survival probabilities and hazard ratios are expressed with 95% confidence limits (CL); confidence intervals that exclude 1 imply significance at at least the 0.05 level. The analyses were undertaken using Statistical Package for Social Sciences (SPSS) and Epidemiological Graphics Estimation and Testing (EGRET) package.

Results

Referral patterns. The age at first referral was considerably younger ($p < 0.00001$) in patients referred from local practitioners without the nature of their condition being recognized

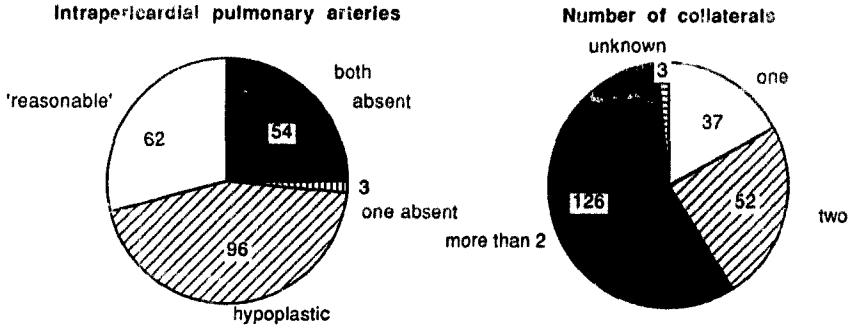

Figure 2. Anatomy of intrapericardial pulmonary arteries and number of congenital systemic-pulmonary collateral arteries (218 patients).

compared with those referred from cardiologists and surgeons for specialist management. (Fig. 1). The 72 patients referred undiagnosed are probably the most representative of the natural presentation of the condition. We must presume that those referred secondarily later in life represent a proportion of those surviving early management elsewhere.

Anatomy. Figure 2 shows the pulmonary artery anatomy and number of systemic-pulmonary collateral vessels when first defined for the whole group of 218 patients. One patient presenting in infancy had additional aortic valve stenosis and liver disease.

There was no statistical relation between the size of the intrapericardial (central) pulmonary arteries and the number of systemic-pulmonary collateral vessels (chi-square 12.9, p = 0.16). There was no difference between patients presenting in infancy or later, between eras or between primary and secondary referrals with respect to pulmonary artery size or number of systemic-pulmonary collateral vessels.

Survival. *Overall survival.* The survival pattern of the group as a whole, reflecting all causes of death (surgical and "natural") is shown in Figure 3. Dividing the time frame into three eras, the survival curves were not significantly different when stratified by the era in which the patients were first seen. At both institutions fewer operations have been undertaken recently, proportionate to the number of patients followed up (from 0.46 to 0.25 operations/patient-year of follow-up before and after 1986, respectively, at Great Ormond Street; from 0.28 to 0.09 operations/patient-year of follow-up at the National Heart Hospital). The numbers of three common categories of operation are shown by year in Figure 4.

Events of infancy. Sixty-five patients were first seen in infancy: 50% of these presented with severe cyanosis (33 patients), 25% with heart failure, and 25% were "well balanced" and had been referred because of a murmur, mild cyanosis or failure to thrive. These proportions were similar in the groups primarily and secondarily referred. The 16 deaths in this age frame correspond to a probability of survival to the first birthday of 60% (95% CL 43 to 73) and an annual hazard of 0.5 (Fig. 5). The events in infancy for the different presentation groups are shown in Figure 6. The infant with aortic valve stenosis and liver disease and four others with critical cyanosis and no intrapericardial pulmonary arteries died without operation. Ten deaths were within 1 month of 46 cardiac operations undertaken in 39 patients. One child with a residual high pulmonary blood flow died of bronchiolitis 5 months after "unifocalization" surgery to reduce overperfusion. The 16

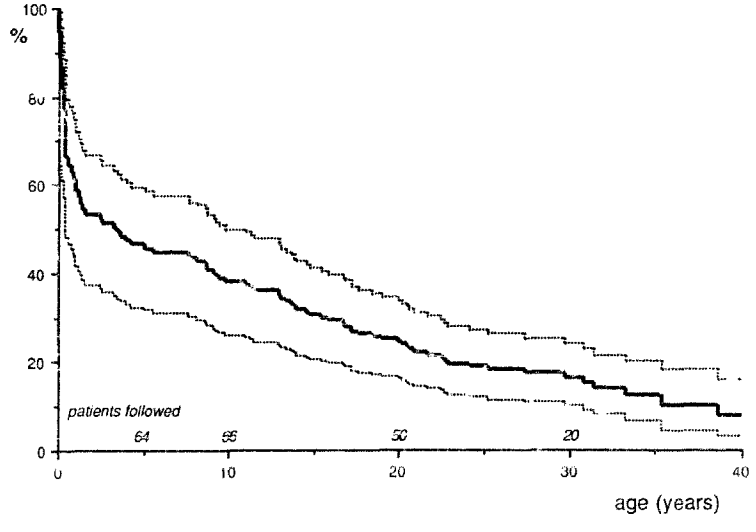

Figure 3. Estimate of overall survival from birth for complex pulmonary atresia (218 patients) with 95% confidence limits (**dotted lines**). (Patients only contribute to the survival curve during the time that they are actually followed up.)

JACC Vol. 25, No. 2
February 1995:491-9

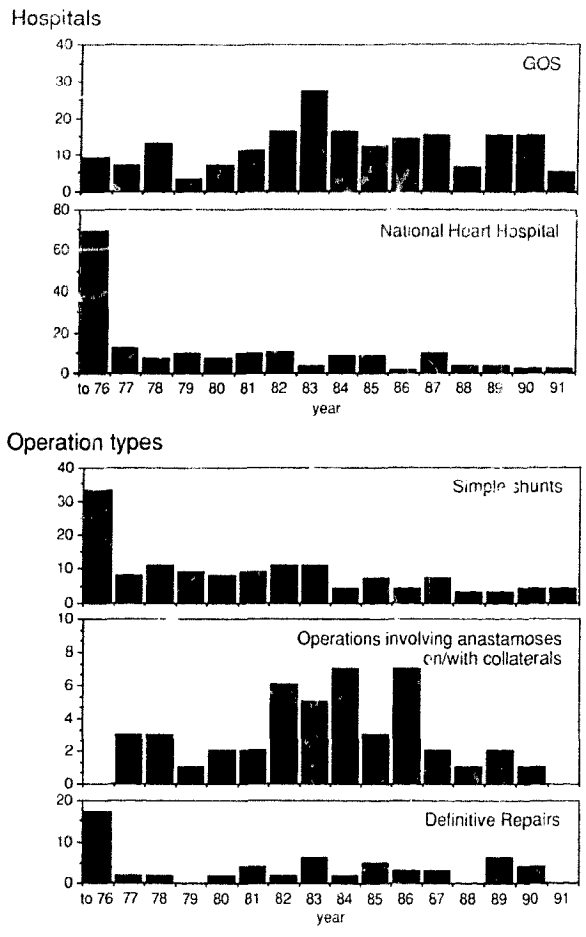

Figure 4. Number of operations (**top**) undertaken at the contributing hospitals during the last 15 years of the study and (**bottom**) overall numbers of three types of operation. GOS = Great Ormond Street Hospital.

patients presenting with heart failure in infancy fared particularly badly, and 10 died by age 2 years. The causes of death in the age frames 0 to 1, 1 to 10 and >10 years are summarized in Table 1. Possible anatomic determinants of survival for each age frame are investigated in Table 2. No influence of intrapericardial pulmonary artery anatomy or number of collateral vessels on survival through infancy was demonstrated.

Age 1 to 10 years. One hundred twenty-seven patients were followed up at some stage or throughout the age range from their 1st to 10th birthday. For patients alive on their 1st birthday, our estimates provide a probability of survival to their 10th birthday of 65% (95% CL 51 to 74) and an annual hazard of 0.11. There were 24 deaths in this age range, 19 within 1 month of 145 cardiac operations in 88 patients. No influence of presenting pulmonary artery size or collateral vessel number on survival through the age frame 1 to 10 years was demonstrated (Table 2).

Age >10 years. One hundred twenty-one patients were followed up at some stage >10 years old. For patients alive on their 10th birthday, our estimates provide a probability of survival to age 35 years of 16% (95% CL 5 to 31). For those alive at age 20 years, the probability of survival to age 35 was 50.6% (95% CL 29 to 68) (Fig. 5). Forty patients >10 years old died, 28 within 1 month of 134 cardiac operations in 79 patients. In this age frame, "reasonable" pulmonary artery anatomy at presentation appeared to be a risk factor for death. This may be because "good" pulmonary artery anatomy was compounded by operation with its high risk.

Patients without operation. For a variety of reasons, 43 patients did not undergo operation: 25 had absent intrapericardial pulmonary arteries; 29 had more than two collateral vessels. Four patients were thought to have inoperable disease (e.g., critical cyanosis and no intrapericardial pulmonary arteries), but most were thought to be too well to justify operation, which had the potential to worsen their condition. Thirty-two patients without operation were alive at follow-up; 10 are >20 years, and the oldest is 45 years old.

Cardiovascular complications. *Endocarditis.* There were 17 episodes of infective endocarditis, the earliest in a 2-year old (1.2 events/100 patient-years of follow-up). Although four episodes occurred in patients who had undergone definitive repair, if the three episodes occurring within 1 year of operation are excluded, definitive repair may be protective in this respect (>1 year after repair, 0.7 events/100 patient-years).

Cerebrovascular events. There were 15 cerebrovascular events (median patient age 10 years, 1 event/100 patient-years). One event occurred in temporal relation to operation; another was fatal.

Aortic regurgitation. The earliest recognition of aortic regurgitation was in a 6-year old. Actuarially, 91% of those patients followed up were free of recognized aortic regurgitation at age 10, 62% at age 20 and 38% at age 30.

Right heart failure. Sixteen patients have had right heart failure, the youngest at age 10. Five patients had right heart failure, four within 1 year of definitive repair or right ventricular outflow tract patching and one within 1 year of a first shunt in a 39-year old patient. There have been four deaths unrelated to definitive repair from this cause.

Effect of elective preliminary operations on survival. The effect on survival of a strategy of elective operation to reorganize the connections of the intrapulmonary arteries with the goal of preparing patients for definitive repair is summarized in Figure 7; 37 patients were affected. This exercise compares patients of the same age before and after initiation of a staging strategy by comparing the annual hazard in the contrasting groups. In infancy, the hazard is excessive in the preoperative group, largely reflecting the deaths of the four patients thought in inoperable condition. Only one of the seven patients whose operation was not dictated by symptomatic status in this age group died early after an elective operation. In the age frames 1 to 10 and 10 to 20 years, the annual hazard of the postoperative patients exceeds that of patients without operation of the same age and presumably similar physiology. The full proportional hazards model examining the implication of elective staging operations beyond infancy on overall survival is shown in Table 3. Once an elective staging operation has been

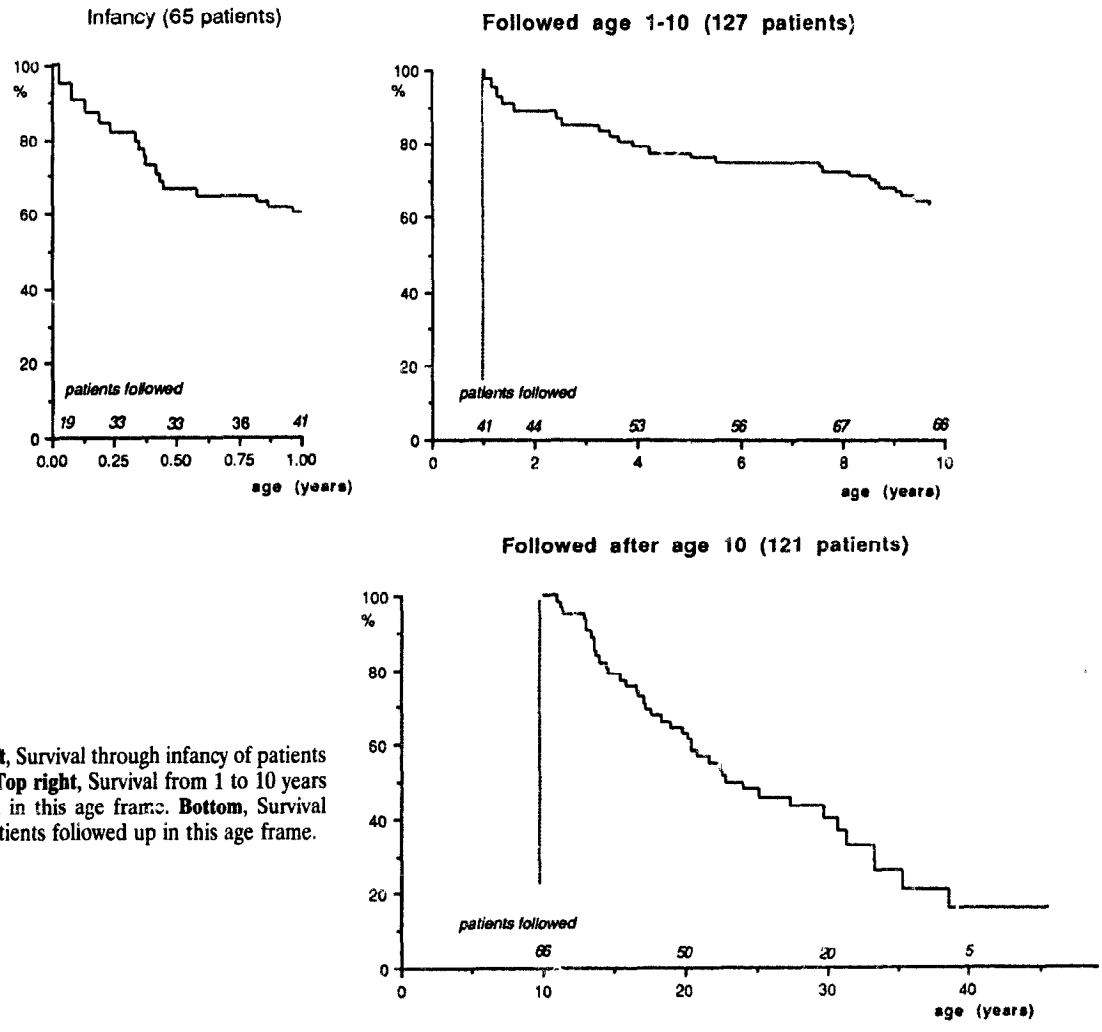

Figure 5. Top left, Survival through infancy of patients seen in infancy. **Top right,** Survival from 1 to 10 years for patients seen in this age frame. **Bottom,** Survival >10 years for patients followed up in this age frame.

performed beyond infancy, postoperative patients had a risk of dying in the subsequent month 8.24 times (95% CL 2.24 to 30.23) that of patients of the same age not yet admitted to such a protocol, allowing for pulmonary artery anatomy, era at presentation, hospital and source of referral. For survivors >2 years after the first elective operation, the hazard had decreased (0.56 compared with patients not yet in a staging protocol), but the confidence intervals were wide (95% CL 0.06 to 5.27), making statements about the advisability of their "investment" uncertain.

Definitive repairs. Fifty-eight definitive repairs involving closure of a ventricular septal defect and connection of the right ventricle to the pulmonary artery with an extracardiac conduit were attempted, with 18 deaths (31%) within 30 days of operation and another 4 within 3 months. Survival beyond definitive repair is summarized in Figure 8. The place of definitive repair was examined by entering the operation as a time-dependent covariate into a Cox proportionate hazards model using all patients who had survived beyond the age of 5 years and incorporating other variables with the potential to influence the shape of the survival curve. The model (Table 4) suggests that patients submitted to definitive operation are at high immediate risk (risk in the subsequent 6 months relative to no repair 43.85 [95% CL 19.72 to 97.5]). This is expected and could still be compatible with definitive repair as a "good investment" for those receiving it, but between 6 months and 2 years the group of postoperative survivors as a whole have not apparently benefited in terms of superior survival relative to patients without surgical correction. Five years after repair, there is some suggestion that survivors of definitive repair might have a better outlook compared with patients without repair, although the figures are not statistically significant. However, when last seen, 62% of survivors were in ability index 1, and 34% were in ability index 2 (6). Only one patient was in index 3, mainly because of chronic right heart failure. Patients surviving definitive repair constitute the majority of those in ability index 1 followed up with this disease.

JACC Vol. 25, No. 2
February 1995:491–9

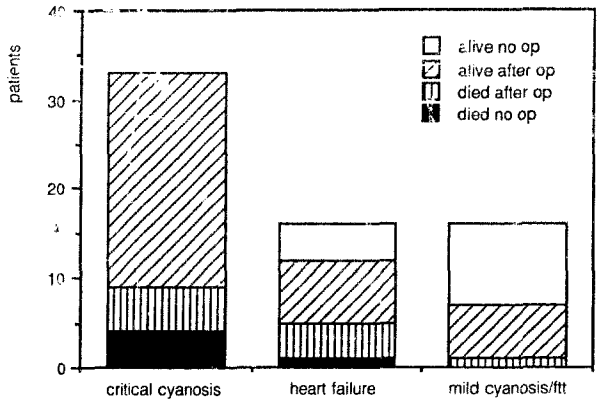

Figure 6. Events during infancy according to reason for presentation. alive = survival for 1 year after presentation; ftt = failure to thrive; op = operation.

Discussion

Our impressions of the natural history of a condition may be biased by the patients we actually see in clinical practice. These patients may not be representative of the condition in general for several reasons. Complex pulmonary atresia is a rare disease. In contrast to pulmonary atresia with a duct-dependent pulmonary blood supply, there is great variability in age at presentation so that specialists with an interest in the cardiology of infancy or adulthood may not appreciate the events at the other extreme of life. Moreover, an institutional interest in the condition can attract referral of patients for a variety of reasons (e.g., "problem" or "good" cases for operation). Although a review that includes a survival curve for 32 patients presenting in infancy is available (9), it seemed worthwhile to attempt a summary of presentation and attrition in complex pulmonary atresia using a large group of patients of all ages.

Pattern of presentation. The contrast between the age at presentation of patients referred undiagnosed and those referred by other cardiologists for specialist management is striking. It seems probable that the subset of 72 patients referred without the nature of their condition being recognized is the most representative of the general pattern of presentation of this condition. If true, ~65% of patients with complex pulmonary atresia present in infancy when 75% of them are severely compromised with either critical cyanosis or heart failure. The remainder present later (including about 10% first diagnosed >10 years old), presumably with a pulmonary flow in infancy that was sufficiently high to make the cyanosis inconspicuous (oxygen saturation at least 85%) but not to make the lungs incompliant and the child symptomatic from heart failure.

In a "complete mixing" situation, such as pulmonary atresia, an oxygen saturation of 85% is achieved by a pulmonary/systemic flow ratio of at least 2.5:1 (mixed venous saturation 60%), and symptoms of heart failure in early childhood probably imply a ratio of ~4:1 or more. Presentation in infancy will tend to occur when patients are outside some "well balanced" range of pulmonary/systemic flow ratio, say 2.5 to 4:1.

Table 1. Causes of Death at Different Ages

	Infancy (n = 65)	Age 1 to 10 yr (n = 127)	Age >10 yr (n = 121)
Critical cyanosis	4	1	
Cardiac operation	10	19	28
Sudden, unexpected		1	1
Heart failure			4
Unknown		2	2
Other	2	1	5
Total	16	24	40

Data presented are number of patients.

Although we may assume that late age at presentation is a proxy for well balanced pulmonary blood flow in infancy, our data find no association of age at presentation with size of the intrapericardial pulmonary arteries or number of systemic-pulmonary collateral vessels. This is not at variance with other reports (10–12) that emphasize the importance of documenting in more detail the systemic-pulmonary collateral vessel sizes as they emerge from the aorta or its branches, their distribution in the lungs and the presence of stenoses along the length of the collateral vessels and within the intrapulmonary vessels. Perhaps presentation beyond infancy implies that neither the systemic-pulmonary collateral nor the hilar and intrapulmonary vessels were very small or stenotic, although the intrapericardial pulmonary arteries could be extremely hypoplastic or entirely absent.

Presentation in infancy. Infancy is the period of greatest attrition for complex pulmonary atresia, without and with attempts at palliation. In this series, >50% of patients diagnosed in infancy underwent operation within days or weeks of presentation because their pulmonary blood flow was considered sufficiently low or high to prejudice survival. The majority underwent operation because of cyanosis. In this age group the hilar vessels, which are the focus of shunt or unifocalization procedures, may be tiny, and poor runoff into the pulmonary bed may have contributed to limiting pulmonary blood flow. The technical difficulties with anastomoses are major. Surgical failures, whether defined in terms of patient deaths or anastomotic occlusions, are common, and there is potential to do harm as well as good. Nevertheless, any surgical focus aiming to make an impact on the overall mortality of this condition must alter the pattern of attrition in infancy.

Recent influential reports (2,3) offer radical alternatives to conventional palliation, but do not address this most difficult group of patients. Iyer and Mee (3) describe 58 patients entered into a program for staged surgical repair designed to encourage growth of the intrapericardial pulmonary arteries and unifocalize the pulmonary blood supply by transplanting or ligating systemic-pulmonary collateral vessels, but only 4 patients had their first operation during infancy. Similarly, Sawatari et al. (2) described the use of complex hilar bridges

Table 2. Proportional Hazards Model for Survival Through Three Age Frames

	Infancy		Age 1 to 10 yr		Age >10 yr	
	Hazard Ratio	95% CL	Hazard Ratio	95% CL	Hazard Ratio	95% CL
No. of collateral vessels						
1	1		1		1	
2	0.28	0.03–3.18	1.17	0.31–4.45	1.32	0.50–3.50
≥3	1.76	0.38–8.17	0.77	0.22–2.77	0.95	0.42–2.17
No central PA	1		1		1	
Hypoplastic central PA	0.73	0.22–2.35	2.96	0.68–12.91	3.26	0.93–11.43
Reasonable central PA	1.01	0.28–3.65	1.55	0.28–8.63	6.84	2.02–23.16

CL = confidence limits; PA = pulmonary artery.

and the remodeling or creation of new intrapericardial pulmonary arteries but undertook the first operation in infancy in only 4 of 34 patients described. It seems unlikely that the pattern of disease presentation is radically different in different countries, so perhaps some very symptomatic patients presenting with cyanosis in infancy were considered unsuitable for entry into the protocols for staged repair. If Sawatari et al. are describing operation only in a subset of patients who generally survived infancy because their pulmonary flow was not at either extreme of the spectrum, this would suggest that neither their systemic-pulmonary collateral nor their hilar or intrapulmonary vessels were very small in the first year of life. This may partly explain their success with complex anastomoses compared with our efforts in infancy.

No new drug becomes available, and no new process is patented and marketed for commercial gain, without tight regulation to guard against inappropriate application. This is not true of novel surgical procedures whose adoption is a matter of judgment for individual professionals (13). To assess the place of a new technique in their own practice, such professionals need specific information about the results of preliminary surgical series, particularly about the patient group operated on (to assess the "generalizability" of the method) and about the outcome achieved. Clearly, late survival and well-being are much the most important outcome measures. However, progress cannot always await long-term studies, so "good" postoperative hemodynamic variables (here primarily low pulmonary artery pressure [14]) must be demonstrable to support optimism about survival.

Our own study also has limitations; it is entirely observational, and the assumptions underlying some of the statistical methodologies contrasting the outlook of patients with and without operation dictate that the answers emerging will not be entirely clear. However, without some perception of the course of patients who do not undergo operation, we cannot address fundamental questions about the place of staging procedures and their long-term consequences. Some conclusions from our data are also prejudiced by the high early postoperative mortality experienced relative to the "best" series reported. However the "investment" provided by staging operations

Figure 7. Estimated annual hazard (with SE) for patients before (preop) and after (postop) an elective first staging operation in preparation for definitive repair.

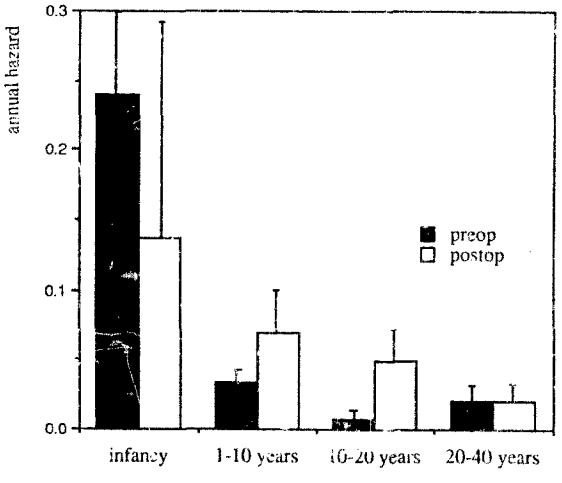

Table 3. Proportional Hazards Model for Survival, Including First Elective Staging Operation as a Time-Dependent Covariate

	Hazard Ratio	95% CL
No elective staging operation	1	
Time after staging operation		
0–1 mo	8.24	2.24, 30.23
1 mo–2 yr	2.42	0.56, 10.43
>2 yr	0.55	0.06, 5.27
Referred undiagnosed	1	
Secondary referrals	0.81	0.11, 6.07
No central PA	1	
Small central PA	0.58	0.18, 1.91
Reasonable central PA	0.58	0.15, 2.29
First seen		
Before 1980	1	
1980–1985	1.32	0.41, 4.22
After 1985	1.78	0.43, 7.40
Hospital 1	1	
Hospital 2	1.40	0.18, 10.47

Abbreviations as in Table 2.

JACC Vol. 25, No. 2
February 1995:491–9

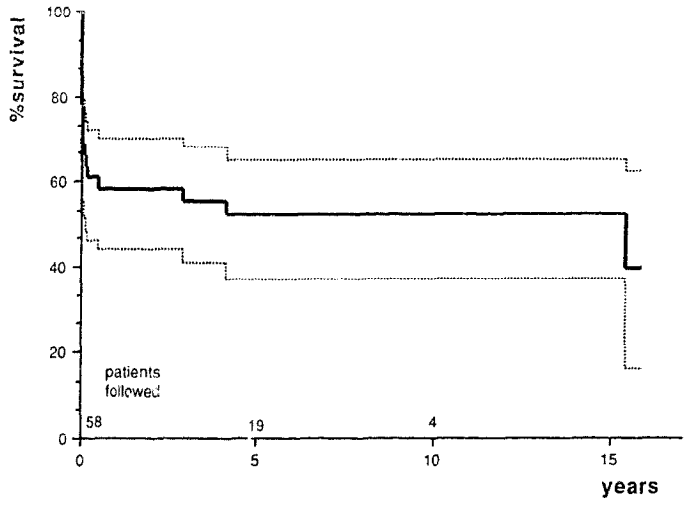

Figure 8. Survival of 58 patients after definitive repair. **Dotted lines** = 95% confidence limits.

even for our survivors has been disappointing. The strategy of electively submitting "well balanced" patients beyond infancy to staging procedures was examined and found wanting: Surgery was the dominant cause of death in every age group. Beyond infancy, patients with "good" pulmonary arteries seemed to fare worse than those with no central pulmonary arteries, presumably because we were tempted to submit them to operation. The annual hazard for patients after a staging strategy is initiated exceeds that of patients in stable condition before such intervention.

Unfortunately, such statements do not resolve the controversy; two polarized positions can still be stated. It can be argued that a program of staging surgery started beyond infancy is started too late and that current strategies, including the use of interventional catheterization, will provide better results than those audited here. Conversely, it could be said that an uncritical reading of the reports of novel surgical procedures for complex pulmonary atresia will adversely influence survival for many patients with this condition by the implication that there is no pulmonary artery anatomy that cannot be surgically "improved." Also, patients surviving infancy are often in stable condition for many years, so that strategies of elective operation would have to be considerably safer and more effective than those available for the past 15 years to provide a good investment for stable patients.

Table 4. Proportional Hazards Model for Survival, Including Definitive Repair as a Time-Dependent Covariate

	Hazard Ratio	95% CL
No definitive repair	1	
After definitive repair		
0–6 mo	43.85	19.72, 97.5
6 mo–5 yr	1.31	0.22, 6.78
>5 yr	0.32	0.04, 2.61
Presenting		
In infancy	1	
At age 2 to 5 yr	6.07	1.65, 22.29
>5 yr	4.09	1.01, 16.53
Referred undiagnosed	1	
Secondary referrals	0.15	0.05, 0.37
No central PA	1	
Small central PA	3.14	1.16, 8.53
Reasonable central PA	3.61	1.26, 10.35
First seen		
Before 1980	1	
1980–1985	1.05	0.47, 2.33
After 1985	0.99	0.2, 4.78
Hospital 1	1	
Hospital 2	1.88	0.69, 5.12

Abbreviations as in Table 2.

Place of definitive repair. There are considerable published data on the contraindications to definitive repair in pulmonary atresia with ventricular septal defect, with emphasis on the importance of the size of the intrapericardial pulmonary arteries for patient selection (15). There has been relatively little focus on the operation as a long-term investment or on the subset of patients with a pulmonary blood supply dependent on systemic-pulmonary collateral vessels.

Our series illustrates the issues faced clinically; ~33% of patients died within 3 months of elective definitive repair. Undoubtedly, some should not have been submitted to surgical intervention, which included closure of the ventricular septal defect according to the most rigorous selection criteria, but the attrition is high nevertheless. However, 2 years postoperatively, survivors of definitive repair still have not realized their investment in terms of improved survival relative to their contemporaries who have not undergone definitive repair. Nonetheless, by 5 years postoperatively, there is some suggestion that their investment is coming to fruition, with a risk of dying of 0.35 relative to patients without definitive repair, although the trend is not statistically unequivocal. In defense of definitive repair is the justification that most survivors are

extremely well and are much less symptomatic than patients who remain with cyanosis.

Conclusions. Over the past 30 years, surgical innovation has vastly widened the spectrum of patients with complex pulmonary atresia to whom definitive relief from cyanosis can be offered. However, matching patient to management, including nonsurgical management, remains the key to optimizing the outlook for life and well-being of individual patients. This study favors the unfashionable conclusion that, as a group, these patients have been overoperated on in our hands. A majority of patients with complex pulmonary atresia present in infancy when operation is difficult, and the novel approaches recently described have not been tested. New techniques and an improved understanding of the determinants of survival through infancy are required if a radical improvement in survival of patients with complex pulmonary atresia is to be achieved.

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